Please add new claims 135-145 as follows.

135. (New) A method for the detection of a nucleic acid in a sample, the method comprising:

a. contacting

a denaturing reagent,

a PNA probe labeled with a detectable moiety, and

a sample comprising a double-stranded nucleic acid having a target sequence complementary to a sequence of the PNA probe

to form a PNA/nucleic acid duplex in the presence of the denaturing reagent which disrupts the secondary structure of the double-stranded nucleic acid but in which the PNA/nucleic acid duplex is stable; and

b. migrating electrophoretically the PNA/nucleic acid duplex in the presence of the denaturing reagent; and

c. detecting the PNA/nucleic acid duplex.

136. (New) The method of claim 135 wherein the detectable moiety is selected from the group consisting of an enzyme, a colored particle, a fluorophore, biotin, a chromophore, a radioisotope, a electrochemical moiety, a chemiluminescent moiety, and fluorescein.

137. (New) The method of claim 135 wherein migrating comprises using a sieving medium.

138. (New) The method of claim 137 wherein the sieving medium comprises at least one material selected from the group consisting of polyacrylamide, agarose, polyethylene oxide, polyvinyl pyrolidine and methylcellulose.

139. (New) The method of claim 135 wherein migrating comprises using a capillary.

140. (New) The method of claim 135 wherein migrating comprises using a channel formed in a substrate.

141. (New) The method of claim 135 wherein the double-stranded nucleic acid comprises strands of greater than 50 nucleotides.

142. (New) The method of claim 135 wherein the denaturing reagent comprises at least one chemical selected from the group consisting of urea, formamide, and an organic solvent.

143. (New) The method of claim 135 wherein the denaturing reagent comprises an ionic buffer.

144. (New) The method of claim 135 wherein the PNA probe comprises a charge-modifying moiety.

145. (New) The method of claim 135 wherein the PNA probe is associated with a particle.

RESPONSE

In view of the extended prosecution history of this application, Applicants have elected to cancel without prejudice all of the pending claims and to introduce new claims 135-145, with claim 135 as the only independent claim. Applicants cancel all of the pending claims without any intention of abandoning the subject matter of the cancelled claims or of disclaiming equivalents thereof. After entry of this Amendment, new claims 135-145 will be pending. In view of the new claims and the following remarks, Applicants respectfully request reconsideration of the rejections and allowance of claims 135-145.

New Claims

Support for new claim 135 is found in the application as filed at least on page 9, line 14 to page 10, line 20; on page 11, lines 9-24; on page 13, lines 3-16; and in originally-filed claims 1, 2, 6, 8, 10, and 11.

Support for new claim 136, corresponding generally to cancelled claims 65, 75-82, and 100-106, is found in the application as filed at least on page 5, lines 6-8; on page 9, lines 10-13; on page 12, line 7; and in originally-filed claim 3 (which is similar to new claim 136).

Support for new claim 137, corresponding generally to cancelled claim 59, is found at least in originally-filed claim 4 (which is similar to new claim 137).

Support for new claim 138, corresponding generally to cancelled claim 60, is found at least in originally-filed claim 5 (which is similar to new claim 138).

Support for new claim 139 is found at least in originally-filed claim 7 (which is similar to new claim 139).

Support for new claim 140 is found in the application as filed at least on page 28, lines 25-26.

Support for new claim 141 is found at least in originally-filed claim 9 (which is similar to new claim 141).

Support for new claim 142, corresponding generally to cancelled claims 61 and 96, is found at least in originally-filed claim 11 (which is similar to new claim 142).

Support for new claim 143, corresponding generally to cancelled claims 62 and 97, is found in the application as filed at least on page 13, lines 3-11.

Support for new claim 144, corresponding generally to cancelled claims 64 and 98, is found in the application as filed at least on page 11, lines 17-18 and page 15, lines 21-30.

Support for new claim 145, corresponding generally to cancelled claim 66, is found in the application as filed at least on page 5, line 8 and on page 12, lines 3-14.

Accordingly, Applicants submit that no new matter is introduced by the new claims.

Objection to the Title

Applicants have amended the title to reflect the methods recited in new claims 135-145. Accordingly, Applicants request withdrawal of this objection.

Rejections Under 35 U.S.C. § 112, First Paragraph

Without reaching the merits of the rejection under 35 U.S.C. § 112, first paragraph, or acquiescing to the rejection, Applicants cancel without prejudice claims 69, 120-122, 128, and 131, thereby rendering their rejection moot.

Applicants believe that the objected-to claim language does not appear in any of new claims 135-145.

Rejections Under 35 U.S.C. §§ 102(b) and 103(a)

Claims 57, 96-98, 110, 115, 127, 128, and 130-133 were rejected under 35 U.S.C. § 102(b) over Rose, Anal. Chem. 65: 3545 (1993) ("Rose"); claims 58, 59, 61, 62, 64, 67, 68, and 71 were rejected under 35 U.S.C. § 103(a) over Rose in view of In re Harza, 274 F.2d 669 (CCPA 1960); and claims 57-62, 64-68, 70, 71, 75-82, 96-98, 100-106, 110, 112, 113, 115, 117-122, 127, 128, and 130-133 were rejected under 35 U.S.C. § 103(a) over Rose in view of In re Harza, 274 F.2d 669 (CCPA 1960) and further in view of U.S. Patent No. 6,045,995 to Cummins *et al.* ("Cummins") and U.S. Patent No. 5,539,082 to Nielsen *et al.* ("Nielsen").

Without reaching the merits of or acquiescing to these rejections, Applicants have cancelled all previously pending claims without prejudice, thereby rendering each of these rejections moot.

Nevertheless, without acquiescing to them, Applicants acknowledge the Patent Office's prior positions regarding Rose and Nielsen and respectfully submit that new independent claim 135 more particularly recites methods of the invention such that Rose, Cummins, and Nielsen, either alone or in combination, do not teach, suggest, or motivate each of the claimed features.

Specifically, new claim 135 recites, in part, contacting a denaturing reagent, a PNA probe labeled with a detectable moiety, and a sample comprising a double-stranded nucleic acid having a target sequence complementary to a sequence of the PNA probe to form a PNA/nucleic acid duplex in the presence of the denaturing reagent which disrupts the secondary structure of the double-stranded nucleic acid but in which the PNA/nucleic acid duplex is stable. Accordingly, the denaturing reagent must disrupt the secondary structure of the double-stranded nucleic acid.

Rose does not disclose the above-underlined feature of new claim 135. Although Figure 7 of Rose does indicate that some small amount of the ODN:PNA heteroduplex forms over approximately two hours, nowhere does Rose report that a denaturing reagent was used to disrupt the secondary structure of the double-stranded nucleic acid. Rather, Rose suggests that strand displacement may occur where, instead of forming a triplex with double-stranded DNA, the PNA displaces the complementary DNA strand and binds to the antiparallel DNA strand. (See Rose, page 3549, column 2, first full paragraph). This mechanism is supported by Nielsen, which suggests that "[u]nexpectedly, [PNA's according to Nielsen] also are able to recognize duplex DNA by displacing one strand, thereby presumably generating a double helix with the other one." (Nielsen, column 6, lines 42-45). Moreover, because the majority of the duplexes in Rose are ODN:ODN duplexes, it seems unlikely that Rose utilizes a denaturing reagent that disrupts the secondary structure of the double-stranded nucleic acid but in which the PNA/nucleic acid duplex is stable. As such, Rose does not teach, suggest, or motivate the recited denaturing reagent or method.

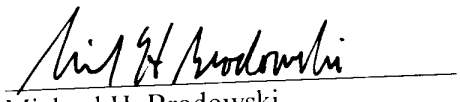
Cummins does not cure this deficiency as it discloses varying temperature to manipulate the binding of PNA to DNA or RNA. (Cummins, column 13, lines 12-24). Nielsen also does not cure this deficiency. Nielsen appears to report on adding PNA to a sample containing single stranded DNA, either with or without the single stranded complement to this DNA being present (*e.g.*, Examples 38 and 81 of Nielsen). Accordingly, Rose, Cummins, and Nielsen, either alone or in combination, fail to teach, suggest, or motivate using a denaturing reagent to disrupt the secondary structure of a double-stranded nucleic acid to permit the formation of a PNA/nucleic acid duplex. Moreover, Rose, Cummins, and Nielsen, either alone or in combination, do not provide the requisite expectation of successfully practicing that which Applicants claim.

Therefore, Applicants submit that claim 135, and the claims dependent therefrom, are novel and unobvious over the cited references.

CONCLUSION

In view of the new claims and remarks presented herein, Applicants submit that claims 135-145 are in condition for allowance and respectfully request that they proceed to issue. As a courtesy to the Applicants, Applicants respectfully request that the Patent Office contact the undersigned attorney at the telephone number indicated below should there be any further issues to address.

Respectfully submitted,



Date: December 31, 2002
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